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Health and Environmental Effects Profile for Brominated Diphenyl Ethers

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR BROMINATED DIPHENYL ETHERS

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
OFFICE OF HEALTH AND ENVIRONMENTAL ASSESSMENT
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
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16. ABSTRACT

The Health and Environmental Effects Profile for Brominated diphenyl ethers was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Pentabromodiphenyl ether, Octabromodiphenyl ether and Decabromodiphenyl ether have been determined to be systemic toxicants. An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for Pentabromodiphenyl ether is 4.4×10^{-4} (mg/kg bw/day), for Octabromodiphenyl ether is 6.2×10^{-4} (mg/kg bw/day) and for Decabromodiphenyl ether is 1×10^{-2} (mg/kg bw/day) for oral exposure.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field Group

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

ACKNOWLEDGEMENTS

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Scientists from the following U.S. EPA offices provided review comments for this document series:

Environmental Criteria and Assessment Office, Cincinnati, OH
Carcinogen Assessment Group
Exposure Assessment Group
Reproductive Effects Assessment Group

Editorial review for the document series was provided by:
Judith Olsen and Erma Durden
Environmental Criteria and Assessment Office, Cincinnati, OH

Technical support services for this document series were provided by:
Bette Zwayer, Pat Daunt, Karen Mann, and Jacky Bohanon
Environmental Criteria and Assessment Office, Cincinnati, OH.

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LIST OF ABBREVIATIONS

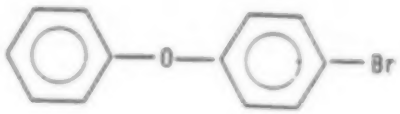
ADI	Acceptable daily intake
GC/MS	Gas chromatography/mass spectrometry
i.p.	Intraperitoneal
LC_{50}	Concentration lethal to 50% of recipients
LD_{50}	Dose lethal to 50% of recipients
LOEL	Lowest-observed-effect level
nm	Nanometers
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect level
ppb	Parts per billion
ppm	Parts per million
TWA	Time-weighted average

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

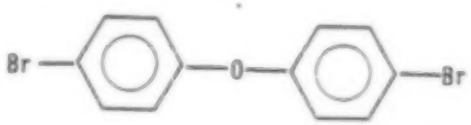
Nine brominated diphenyl ethers (or diphenyl oxides) are the subject of this hazard profile. The structure, molecular formula, molecular weight, Chemical Abstracts Service (CAS) Registry number and common synonyms for the subject chemicals are summarized below:-

p-Bromodiphenyl ether:



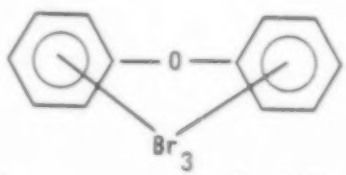
Molecular formula:	$C_{12}H_9BrO$
Molecular weight:	249.11
CAS No.:	101-55-3
Synonyms:	1-Bromo-4-phenoxybenzene p-Bromophenylphenyl ether 4-Bromodiphenyl ether 4-Bromophenyl ether

p,p'-Dibromodiphenyl ether



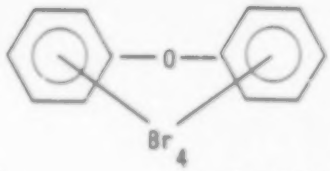
Molecular formula:	$C_{12}H_8Br_2O$
Molecular weight:	328.02
CAS No.:	2050-47-7
Synonyms:	Bis(p-bromophenyl)ether Bis(4-bromophenyl)ether

Tribromodiphenyl ether



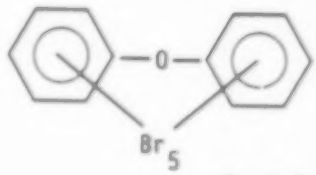
Molecular formula:	$C_{12}H_7Br_3O$
Molecular weight:	407.1
CAS No.:	49690-94-0
Synonyms:	Benzene, 1,1'-oxybis-, tribromo-derivative

Tetrabromodiphenyl ether



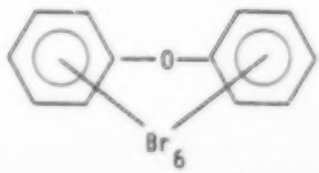
Molecular formula:	$C_{12}H_6Br_4O$
Molecular weight:	485.82
CAS No.:	4088-47-9
Synonyms:	Benzene, 1,1-oxybis-, tetrabromo-derivative

Pentabromodiphenyl ether



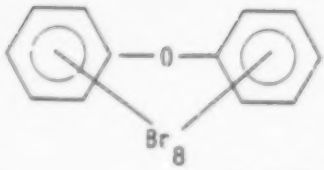
Molecular formula:	$C_{12}H_5Br_5O$
Molecular weight:	564.72
CAS No.:	32534-81-9
Synonyms:	Benzene, 1,1'-oxybis-, pentabromo-derivative; DE71

Hexabromodiphenyl ether



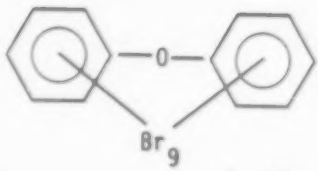
Molecular formula:	$C_{12}H_4Br_6O$
Molecular weight:	643.62
CAS No.:	36483-60-0
Synonyms:	Benzene, 1,1'-oxybis-, hexabromo-derivative; BR 33N

Octabromodiphenyl ether.



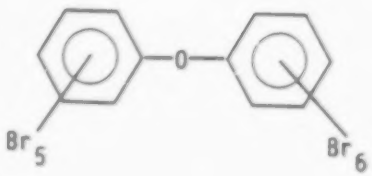
Molecular formula:	$C_{12}H_2Br_8O$
Molecular weight:	801.42
CAS No.:	32536-52-0
Synonyms:	Benzene, 1,1'-oxybis-, octabromo-derivative; Phenyl ether, octabromo derivative Bromkal 79-8DE; DE 79; FR 143; Tardex 80

Nonabromodiphenyl ether



Molecular formula:	$C_{12}HBr_9O$
Molecular weight:	880.32
CAS No.:	63936-56-1 68928-79-0 66169-95-7
Synonyms:	Benzene, pentabromo(tetrabromophenoxy)-

Decabromodiphenyl ether



Molecular formula:	$C_{12}Br_{10}O$
Molecular weight:	959.22
CAS No.:	1163-19-5
Synonyms:	Benzene, 1,1'-oxybis(2,3,5,6-penta-bromo-) Ether, bis(pentabromophenyl); Decabromophenyl oxide; Decabromophenyl ether; BR 55N, Bromkal 82-0DE; Bromkal 83-10DE; Pentabromophenyl ether

1.2. PHYSICAL AND CHEMICAL PROPERTIES

The general physical and chemical properties of p-bromodiphenyl ether (Ca lahan et al., 1979; Mabey et al., 1982), p,p'-dibromodiphenyl ether (Weast, 1977) and decabromodiphenyl ether (Norris et al., 1973) are summarized below. Data regarding the properties of the other designated brominated diphenyl ethers were not located in the literature searched (see Appendix).

p-Bromodiphenyl ether

Melting point:	18.72°C
Boiling point:	310.14°C
Vapor pressure at 20°C:	0.0015 mm Hg
Water solubility at 25°C (calculated):	4.8 mg/ℓ
Octanol/water partition coefficient (calculated):	12,000-87,000

p,p'-Dibromodiphenyl ether:

Melting point:	60.5°C
Boiling point:	338-340°C
Density:	1.8 (solution)
Water solubility:	not available

Decabromodiphenyl ether:

Melting point:	290-306°C
Density:	3.84 (Larson, 1979)
Water solubility at 25°C:	20-30 ppb
Solubility in other solvents:	
cottonseed oil:	600 ppm
acetone:	0.05 g/100 g
benzene:	0.48 g/100 g
chlorobenzene:	0.60 g/100 g
methylene bromide:	0.42 g 100 g
methylene chloride:	0.49 g/100 g
o-xylene:	0.87 g/100 g
Octanol/water partition coefficient:	172,000

1.3. PRODUCTION DATA

Brominated diphenyl ethers/oxides are prepared by the bromination of diphenyl oxide in the presence of a Friedel-Crafts catalyst (Larson, 1979). These compounds are produced by the chemical companies listed in Table 1-1 (SRI, 1983; U.S. EPA, 1977) (Table 1-1).

1.4. USE DATA

The brominated diphenyl ethers are generally used as flame retardant additives for plastic resins (Larson, 1979).

TABLE 1-1

Production Data for Brominated Diphenyl Ethers*

Chemical	Firm	Location	Quantity (lbs/year)
p-Bromodiphenyl ether	Velsicol Chemical Corp.	Chicago, IL	NR
	Columbia Organic Chemical Co.	Columbia, SC	<1000
p,p'-Dibromodiphenyl ether	NA	NA	NA
Tribromodiphenyl ether	NA	NA	NA
Tetrabromodiphenyl ether	NA	NA	NA
Pentabromodiphenyl ether	Great Lakes Chemical Corp.	El Dorado, AR	NR
	White Chemical Corp.	Bayonne, NJ	NR
Hexabromodiphenyl ether	Great Lakes Chemical Corp.	West Lafayette, IN	NR
Octabromodiphenyl ether	Great Lakes Chemical Corp.	El Dorado, AR	NR
	White Chemical Corp.	Bayonne, NJ	NR
Nonabromodiphenyl ether	Great Lakes Chemical Corp.	El Dorado, AR	NR
Decabromodiphenyl ether	Dow Chemical Corp.	Midland, MI	1,000,000-10,000,000
	Great Lakes Chemical Corp.	El Dorado, AR	NR
	Hexcel Fine Organics	Chatsworth, CA	1,000,000-10,000,000
	Ethyl Corp.	Magnolia, AR	NR
		Sayreville, NJ	

*Source: SRI, 1983; U.S. EPA, 1977

NA = Not available; NR = Not reported

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

Limited data are available on the fate and transport of the brominated diphenyl ethers in the environment. The preponderance of data pertain to the fate of the compounds in water and suggest that degradation in water is likely to occur slowly via photochemical reactions.

Norris et al. (1973) speculated that the brominated diphenyl ethers will degrade in water via a photohydroxylation process leading to the formation of phenolic compounds. Once photodegradation is initiated, it should accelerate as electron withdrawing bromines are replaced by electron releasing hydroxyls. Also, as hydroxyl replacement of bromine proceeds, the resulting species would be expected to absorb more strongly in the longer wavelengths and this could ultimately result in the rupturing of the aromatic ring (Norris et al., 1973).

Norris et al. (1973) exposed distilled water saturated with excess decabromodiphenyl oxide (1.25 g/ℓ) to sunlight for 98 days. A significant increase in bromine concentration was found relative to an unexposed 98-day sample, but GC/MS analyses showed that the photodegradation products were not lower brominated diphenyl oxides (i.e., p-bromo-, p,p'-dibromo- or mixed tribromodiphenyl oxides). After 98 days, the concentration of bromine in the water (7.3 ppm) reportedly corresponded to ~300 times the initial amount of decabromodiphenyl oxide that was soluble in the water, but information on the rate of photolysis in the water was not provided. Dorfman and Adams (1973) considered that the photolytic interaction of hydroxyl radical with the aromatic ring of p-bromodiphenyl ether is too slow in water to be environmentally significant.

Direct photolysis of brominated biphenyl ethers may be expected to occur to some extent since p-chlorodiphenyl ether absorbs the ultraviolet region

of the ground-level solar spectrum (i.e., absorption maxima at 272, 279 and 293 nm), but the information for estimating the rates of direct photolysis an aquatic environment are not available (Callahan et al., 1979). Hydrolysis of any of the covalent bonds of the brominated diphenyl ethers at ambient environmental conditions is considered unlikely, since the negative charge-density of the aromatic ring will impede the nucleophilic attack of water or hydroxide ion (Callahan et al., 1979).

The mass transfer coefficient for volatilization of p-chlorodiphenyl ether from water has been calculated to be 7.0 cm/hour (Branson, 1977). The half-life for volatilization of p-chlorodiphenyl ether from 1 m deep water is estimated from this coefficient to be ~10 hours, and a similar value can be expected for structurally analogous p-bromodiphenyl ether (Callahan et al., 1979). Limited vapor pressure (see Section 1.2.) and experimental data suggest that the higher bromodiphenyl ethers are less volatile from water. Norris et al. (1973) found no change in the concentration (18 ppb) of decabromodiphenyl ether in water stored in a tank over a period of 48 hours, indicating no loss by volatilization or adsorption upon the surface of the tank.

The estimated evaporative half-life of ~10 hours for p-bromodiphenyl ether should be considered a minimum value since a calculated octanol/water partition coefficient (log P=4.28) for this compound and monitoring data (Chapter 3) suggest that it is likely that sorption by organic particles and suspended clays (e.g., sediments) will occur (Leo et al., 1971). Sorption of p-bromodiphenyl ether by suspended organic material is further indicated by a sediment to water distribution ratio of 4:1 for p-chlorodiphenyl ether during biodegradation studies with sludge (Branson, 1977). Sorption is

expected to increase with increasing degree of bromination due to presumed decreased water solubility, increased octanol-water partition coefficients and decreased volatilization.

Limited experimental data indicate that biodegradation of p-bromodiphenyl ether is not likely to occur to an appreciable extent in water, even after microbial acclimation. Yagi and Sudo (1980) found that Alcaligenes BM-2, a strain of soil bacteria capable of using PCB (di-Cl) mixtures as the sole source of carbon, did not grow when p-bromodiphenyl ether or p,p'dibromodiphenyl oxide were used as sole carbon sources. In static culture flask-screening assays, 5 and 10 mg/ℓ aqueous solutions of p-bromodiphenyl ether were incubated at 25°C in the dark with domestic wastewater as the microbial inoculum in glass-stoppered bottles to minimize volatilization (Tabak et al., 1981). Analyses for the parent compound as well as dissolved organic carbon and total organic carbon, after 7 days incubation followed by the redosing of three weekly subcultures (28 days total incubation), showed that significant biodegradation did not occur. Degradation was also not observed in a similarly designed static flask assay with 5 mg/ℓ p-bromodiphenyl ether and settled domestic sewage inocula (Patterson and Kodukala, 1981). p-Bromodiphenyl ether has been reported to be 95% degraded when introduced as a pollutant (360 µg/ℓ) in a full-scale activated sludge treatment system (U.S. EPA, 1980a), but this finding should not be considered indicative of biodegradation in water because the microbial population in activated sludge is expected to be much higher than those in ambient aquatic media.

The relatively high octanol/water partition coefficient for p-bromodiphenyl ether (calculated log P=4.28) (Callahan et al., 1979) suggests a potential for bioaccumulation in aquatic ecosystems. Although it is

expected that the potential for bioaccumulation would increase with an increasing degree of bromine substitution, Norris et al. (1973) found that decabromodiphenyl ether did not bioconcentrate to a measurable extent in the tissues of Rainbow trout that were exposed to the ^{14}C-labeled compound under static conditions for up to 48 hours. Analysis of water concentrations and tissue levels indicated that while decabromodiphenyl ether did not bioconcentrate, the positive control 2,2'4,4'-tetrachlorobiphenyl had bioconcentrated at least 50 times within 4 hours.

Although the extent of volatilization of the brominated diphenyl ethers from surface waters into the atmosphere is probably very low, it is expected that any of the compounds that enter the troposphere will be subject to photodegradation, and possible sorption to particulate matter with either dry or wet deposition. Information summarized in the aquatic fate/ transport paragraphs suggests that brominated diphenyl ethers that come into contact with the soil will not significantly leach (due to sorption and water insolubility, particularly in soils with high organic matter and/or clay contents), volatilize or biodegrade. However, due to the presumed high sorption of the brominated diphenyl ethers photodegradation could occur at the soil surface.

3. EXPOSURE

STORET contains numerous monitoring data for p-bromodiphenyl ether in total water (2193 listings), sediment (686 listings) and aquatic organism tissue (346 listings). The mean concentrations of p-bromodiphenyl ether in these media are 0.2 mg/ℓ (range, 0-202.7 mg/ℓ), 3.5 mg/kg (range, 0-380.0 mg/kg) and 2.0 mg/kg (range, 0-70.0 mg/kg), respectively. It should be noted, however, that a qualitative analysis of the data indicated that the measurements reflect a preponderance of river water samples taken in the vicinity of or downstream from industrial effluent discharges with an insufficient number of groundwater and community drinking water samples. Additionally, much of the reported data is remarked (remark code K - less than values). No monitoring data for the other brominated diphenyl ethers are listed in STORET, but the higher brominated compounds (i.e., tetra- to decabromodiphenyl ethers) were qualitatively identified by GC/MS in sludge samples obtained from an industrial discharge-treatment zone in New Jersey (DeCarlo, 1979).

Decabromodiphenyl ether has been qualitatively identified by GC/MS in air particulate and soil samples from Arkansas (DeCarlo, 1979), but additional monitoring data for the brominated biphenyl ethers in these media are not available. Data on the levels of brominated biphenyl ethers in food were not found, and the general lack of monitoring data precludes evaluation of the importance of dermal exposures to total exposure. Decabromodiphenyl ether was detected at levels as high as 5 µg/kg in composite samples of human hair obtained from barber shops in El Dorado and Magnolia, AR, which produce this chemical (DeCarlo, 1979), indicating that potentially significant exposures via the inhalation, oral and/or dermal routes can occur.

4. COMPOUND DISPOSITION AND PHARMACOKINETICS

4.1. ABSORPTION

Decabromodiphenyl ether does not appear to be absorbed to a great extent from the gastrointestinal tract. Following the oral administration of 1.0 mg/kg ^{14}C-decabromodiphenyl ether in corn oil to male and female Sprague-Dawley rats, Norris et al. (1973, 1975), reported 90.6% of the ^{14}C-activity in the feces within 24 hours post-treatment and >99% of the administered ^{14}C-activity in the feces 48 hours post-treatment. Small amounts of decabromodiphenyl ether were absorbed via the gastrointestinal tract; however, only 1% of the ^{14}C-activity was detected in the urine and expired air of treated animals. There was a limited distribution of ^{14}C-activity into other tissues.

4.2. DISTRIBUTION

Norris et al. (1973, 1975) administered 1.0 mg/kg ^{14}C-labeled decabromodiphenyl ether orally in a corn oil vehicle to 3 male and 3 female Sprague-Dawley rats. Sixteen days after dosing, the ^{14}C-label was detected in adrenal and splenic tissue at levels of 0.01 ± 0.06 and 0.06 ± 0.07% of the dose administered/g of tissue, respectively. No ^{14}C activity was observed in the adipose tissue, heart, skin, liver or pancreas of treated animals.

In a 2-year chronic oral study by Dow Chemical U.S.A. (Kociba et al., 1975; Norris et al., 1973, 1975), male and female Sprague-Dawley rats were fed diets containing decabromodiphenyl ether at dosages of 0, 0.01, 0.1 or 1.0 mg/kg/day. After 180 days of treatment at the 0.1 and 1.0 mg/kg/day level treated animals had significantly increased ($P<0.05$) adipose tissue levels of bromine when compared to control animals. During the second year of treatment, bromine levels in adipose tissue of the 0.1 and 1.0 mg/kg/day

rats continued to rise in a dose-related manner. Levels of bromine in the liver slightly increased at the 1.0 mg/kg/day dosage while levels in the kidney, muscle and serum were not affected.

4.3. METABOLISM

Pertinent data regarding the metabolism of the selected brominated diphenyl ethers were not located in the available literature.

4.4. EXCRETION

Norris et al. (1973, 1975) administered a single oral dose of ^{14}C-labeled decabromodiphenyl ether in a corn oil suspension at a level of 1.0 mg/kg to 3 male and 3 female Sprague-Dawley rats. The feces was the principal route of excretion, with 90.6 and >99% of the administered dose excreted in the feces within 24 and 48 hours, respectively. Small amounts (<1%) of the administered dose were excreted in the urine and expired air of treated animals.

5. EFFECTS

5.1. CARCINOGENICITY

Both sexes of Sprague-Dawley rats (25/sex/dose level) were administered dietary concentrations of decabromodiphenyl ether in dosages of 0, 0.01, 0.1 or 1.0 mg/kg/day for 2 years (Kociba et al., 1975; Norris et al., 1973, 1975). Neither treatment-related carcinogenic effects nor increased tumor incidences were observed for either sex or treatment group.

Decabromodiphenyl ether is currently being tested for carcinogenicity by the National Toxicology Program (NTP, 1982). The compound is being administered in the diet to rats and mice; histopathologic analysis is in progress.

Theiss et al. (1977) tested p-bromodiphenyl ether in the Strain A mouse pulmonary tumor assay. Groups of 20 Strain A/St male mice were given 23, 17 or 18 i.p. injections of p-bromodiphenyl ether in tricaprylin at dose levels of 40, 100 or 200 mg/kg, respectively. Under these test conditions, p-bromodiphenyl ether gave a negative response in the pulmonary tumor assay. The number of tumors/mouse and survival rates of treated animals were not significantly different from control values.

5.2. MUTAGENICITY

Pertinent data on the mutagenic effects of brominated diphenyl ethers were not located in the available literature. However, the reproductive studies of Norris et al. (1973, 1975) are noteworthy. Female Sprague-Dawley rats were administered dietary concentrations of decabromodiphenyl ether at dosages of 0, 3, 30 or 100 mg/kg/day for 90 days prior to mating and continueing through gestation and lactation. No increases in cytogenetic aberrations were observed in the bone marrow cells from exposed neonates, when compared to control values.

5.3. TERATOGENICITY

Norris et al. (1973, 1975) administered decabromodiphenyl ether in a corn oil suspension by gavage at dose levels of 0, 10, 100 or 1000 mg/kg to pregnant Sprague-Dawley rats on days 6 through 15 of gestation. There was no maternal toxicity or teratogenic response at any dose level tested. Fetotoxicity, as evidenced by a significantly increased incidence of resorptions was observed at the lower dose levels, but not at the highest dose level. At the highest dose level, an increased incidence of subcutaneous edema and delayed ossification of normally developed bones of the skull were found among litters. The authors did not enumerate the incidences of these fetal effects, nor did they report how many rats were tested.

5.4. OTHER REPRODUCTIVE EFFECTS

Norris et al. (1973, 1975) administered decabromodiphenyl ether at dietary levels of 0, 3, 30 or 100 mg/kg/day to female Sprague-Dawley rats for 90 days prior to mating and continuing through gestation and lactation. The number of animals/group was not specificed. No treatment-related effects on reproductive capacity, lactation indices or neonates were observed. There was no increase in cytogenetic aberrations in bone marrow cells from exposed neonates when compared to controls.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

In a 2-year chronic oral study, Norris et al. (1973, 1975) and Kociba et al. (1975) administered decabromodiphenyl ether to Sprague-Dawley rats (25/sex/dose) at dietary concentrations that provided doses of 0, 0.01, 0.1 or 1.0 mg/kg/day. At these relatively low levels of administration, neither treatment-related deaths nor effects on body or organ weight changes, or hematologic, pathologic or urinalysis indices were observed. Additional

groups of 10-34 rats/sex/dose were treated in the same manner and were sacrificed at intervals for analysis of tissue bromine levels. Results of these analyses are discussed in Chapter 4 of this profile.

In another oral study, male Sprague-Dawley rats were fed decabromodiphenyl ether in their diet at dosages of 0, 8, 80 or 800 mg/kg/day for 30 days (Norris et al., 1973, 1975). No treatment-related changes in body weight, appearance, demeanor or measured hematological or urinalyses indices were observed. At the 80 and 800 mg/kg/day levels, liver weights were increased; however, there was no change in heart, testes, brain or kidney weights at any dose tested. Upon histopathological examination, liver and kidney lesions were noted in animals ingesting 800 mg/kg/day; the hepatic lesions were characterized by centrilobular cytoplasmic enlargement and vacuolation, while renal lesions were characterized by hyaline degenerative cytoplasmic changes. Thyroid hyperplasia was observed in animals that were administered decabromodiphenyl ether at either 80 or 800 mg/kg/day. No histopathological changes were seen in animals treated at the 8 mg/kg/day level.

Pentabromodiphenyl ether and octabromodiphenyl ether in corn oil were administered by gavage to unspecified numbers of male Sprague-Dawley rats for 90 days (Carlson, 1980a). Two dose regimes were used, a high dose series of 0, 6.25, 12.5 or 25 µmol/kg/day (equivalent doses of 0, 3.53, 7.06 or 14.11 mg pentabromodiphenyl ether/kg/day and 0, 5.01, 10.02 or 20.03 mg octabromodiphenyl ether/kg/day) and a low dose series of 0, 0.78, 1.56 or 3.13 µmol/kg/day (equivalent doses of 0, 0.44, 0.88 or 1.77 mg pentabromodiphenyl ether/kg/day and 0, 0.62, 1.25 or 2.51 mg octabromodiphenyl ether/kg/ day). Treated rats were observed for the effect of pentabromodiphenyl ether and octabromodiphenyl ether on the induction of O-ethyl

O-p-nitrophenyl phenylphosphonothioate (EPN) detoxification, p-nitroanisole demethylation, cytochrome c reductase and cytochrome P-450. Liver enzyme induction occurred at doses of $\geq$0.78 µmol/kg/day for both compounds. Some of these changes were persistent, lasting for 30-60 days after the cessation of treatment. No histological liver abnormalities were observed in rats treated with either compound at 0, 0.78, 1.56 or 3.13 µmol/kg/day.

5.6. OTHER RELEVANT INFORMATION

The LD_{50} for p,p'-dibromodiphenyl ether in mice (i.p.) is 125 mg/kg (NIOSH, 1983).

Norris et al. (1973, 1975) evaluated the acute oral and dermal toxicity of decabromodiphenyl ether and observed that this compound exhibits a low acute oral toxicity in rats and a low skin absorption toxicity in rabbits. Female Sprague-Dawley rats were administered a single dose of a 10% corn oil suspension of decabromodiphenyl ether via gastric intubation at levels of 126, 252, 500, 1000 or 2000 mg/kg. No signs of toxicity or gross pathological changes occurred at any dose level during the 14-day observation period post-treatment.

Norris et al. (1973, 1975) applied decabromodiphenyl ether (dry compound) to the shaved skin of New Zealand white rabbits. When the compound was applied for 24 hours to intact skin there was no response, while application for 24 hours to abraded skin resulted in a slight erythematous and edematous response. Application of decabromodiphenyl ether for 5 days/week for 2 weeks to intact skin or for 3 days to abraded skin both yielded slight erythematous and edematous responses. These responses were transient, with the skin returning to normal after cessation of treatment in all cases. None of the treatments had an effect on body weight, appearance or demeanor.

Decabromodiphenyl ether, applied as a dry solid, caused transient irritation of the conjunctival membranes of both washed and unwashed eyes of New Zealand albino rabbits (Norris et al., 1973, 1975). The cornea, iris and lens were not affected by treatment. No skin sensitization in humans (N=50) was induced by the surface application of a homogenous 5% suspension of decabromodiphenyl ether in petroleum 3 times/week for 3 weeks, or on challenge 2 weeks following the final treatment (Norris et al., 1973, 1975).

Koster et al. (1980) assessed the porphyrinogenic action of decabromodiphenyl ether and octabromodiphenyl ether. The compounds were dissolved or suspended in DMSO and incubated in chick embryo liver cell cultures. Decabromodiphenyl ether at a concentration of 5 µg/mℓ medium had no porphyrinogenic action, whereas octabromodiphenyl ether at a concentration of 10 µg/mℓ medium was strongly porphyrinogenic. The pretreatment of chick embryo cell cultures with β-naphthoflavone for 20 hours yielded similar results.

Carlson (1980b) reported that p,p'-dibromodiphenyl ether, pentabromodiphenyl ether, octabromodiphenyl ether and decabromodiphenyl ether induced xenobiotic metabolism in male Sprague-Dawley rats when administered orally in corn oil at a dose of 0.1 mmol/kg/day for 14 days.

6. AQUATIC TOXICITY

6.1. ACUTE TOXICITY

The effects of acute exposure to p-bromodiphenyl ether have been studied in several species of fish and the water flea (Table 6-1). Applegate et al. (1957) reported that 24-hour exposures at 5.0 mg p-bromodiphenyl ether/ℓ caused three species of fish, rainbow trout, bluegill sunfish and sea lamprey, to show signs of stress, but no additional effects were noted (U.S. EPA, 1983). The static LC_{50} values for 24, 48, 72 and 96-hour exposures in the bluegill sunfish, Lepomis macrochirus, were 50.9, 9.62, 4.94 and 4.94 mg/ℓ, respectively (U.S. EPA, 1978; Buccafusco et al., 1981). During this study a precipitate was observed to form in test solutions. Note that the water solubility of p-bromodiphenyl ether has been calculated to be ~4.8 mg/ℓ (Mabey et al., 1982); therefore, reported LC_{50} values exceeding this value probably underestimate the acute toxicity of this compound. The 96-hour NOEL was reported to be <2.80 mg/ℓ for the sunfish (U.S. EPA, 1978). The water flea, Daphnia magna, was less resistant to p-bromodiphenyl ether exposure than any fish species tested. The 24- and 48-hour LC_{50} values for Daphnia magna were 0.46 and 0.36 mg/ℓ, respectively (U.S. EPA, 1978; LeBlanc, 1980). The 48-hour NOEL was <0.046 mg/ℓ (U.S. EPA, 1978).

6.2. CHRONIC TOXICITY

In an early-life-stage (embryo-larval) test conducted with p-bromodiphenyl ether and the fathead minnow, adverse effects on survival and growth were observed. The geometric mean of the highest no-effect and lowest effective levels was 0.122 mg/ℓ (U.S. EPA, 1980b). Pertinent data regarding the effects of chronic exposure to any other brominated diphenyl ether in aquatic organisms could not be located in the available literature.

TABLE 6-1

Acute Toxic Effects of p-Bromodiphenyl Ether to Aquatic Organisms

Species	Duration (hours)	Mean Concentration (mg/ℓ)	Method	Effect	Reference
Rainbow trout, *Salmo gairdneri*	24	5.0	static-aerated	stress observed	Applegate et al., 1957
Bluegill sunfish, *Lepomis macrochirus*	24	5.0	static-aerated	stress observed	Applegate et al., 1957
Bluegill sunfish, *Lepomis macrochirus*	24	50.9	static	LC_{50}	U.S. EPA, 1978; Buccafusco et al., 1981
	48	9.62	static	LC_{50}	U.S. EPA, 1978
	72	4.94	static	LC_{50}	U.S. EPA, 1978
	96	4.94	static	LC_{50}	U.S. EPA, 1978; Buccafusco et al., 1981
	96	<2.80	static	no effect	U.S. EPA, 1978
Sea lamprey, *Petromyzon marinus*	24	5.0	static-aerated	stress observed	Applegate et al., 1957
Water flea, *Daphnia magna*	24	0.46	static	LC_{50}	U.S. EPA, 1978; Le Blanc, 1980
	48	0.36	static	LC_{50}	U.S. EPA, 1978; LeBlanc, 1980
	48	<0.046	static	no effect	U.S. EPA, 1978

6.3. PLANT TOXICITY

Pertinent data regarding the toxic effects of brominated diphenyl ethers on algae and other aquatic plants were not located in the available literature.

6.4. RESIDUES

Bioconcentration studies with rainbow trout, Salmo gairdneri, exposed to decabromodiphenyl- and octabromodiphenyl ether at 0.02 mg/ℓ indicate that little uptake occurs in this species (Norris et al., 1973). Analysis of fish flesh from trout exposed for up to 48 hours indicated that minimal bioconcentration of both compounds had occurred.

6.5. OTHER RELEVANT INFORMATION

Additional information regarding the effects of brominated diphenyl ethers in the aquatic environment could not be located in the available literature.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

The American Industrial Hygiene Association (AIHA, 1981) has established a recommended Workplace Environmental Exposure Level (WEEL) for decabromodiphenyl ether of 5 mg/m^3 as an 8-hour TWA for a 40-hour week.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of brominated diphenyl ethers were not located in the available literature.

8. RISK ASSESSMENT

Decabromodiphenyl ether was tested for carcinogenicity in rats at relatively low dietary levels of 0, 0.01, 0.1 or 1.0 mg/kg/day for 2 years (Kociba et al., 1975; Norris et al., 1973, 1975). No evidence of carcinogenicity was observed. Negative results were obtained for p-bromodiphenyl ether in the Strain A mouse pulmonary adenoma assay (Theiss et al., 1977).

Norris et al. (1973, 1975) observed fetotoxicity but not maternal toxicity or teratogenic effects following gavage administration of decabromodiphenyl ether at dose levels of 0, 10, 100 or 1000 mg/kg to pregnant rats on days 6 through 15 of gestation. Norris et al. (1973, 1975) administered decabromodiphenyl ether at dietary levels of 0, 3, 30 or 100 mg/kg to rats for 90 days prior to mating, continuing through gestation and lactation. No treatment-related effects on reproductive capacity, lactation indices or neonates were observed. There was no increase in cytogenetic aberrations in bone marrow cells from neonates when compared to control values.

Decabromodiphenyl ether was also tested in a 2-year dietary chronic toxicity study in rats at the same dose levels used in the carcinogenicity assay (Kociba et al., 1975; Norris et al., 1973, 1975). A free-standing NOAEL of 1.0 mg/kg/day was established for decabromodiphenyl ether. Generally, an ADI value should not be derived from a free-standing NOAEL; however, corroborative evidence from similarly devised short-term studies by Norris et al. (1973, 1975) makes this calculation appropriate. In the 30-day oral study, male rats were administered decabromodiphenyl ether at dietary concentrations of 0, 0.01, 0.1 or 1.0% (approximate doses of 0, 8, 80 or 800 mg/kg/day) (Norris et al., 1973, 1975). Increased liver weights and thyroid hyperplasia were observed at 80 and 800 mg/kg/day, while liver and kidney lesions were noted only in animals ingesting 800 mg/kg/day. A

level of 8 mg/kg/day can be considered a NOAEL for 30-day exposure to decabromodiphenyl ether. An uncertainty factor of 10 must be applied to convert from a subchronic to a chronic dose value, setting the NOAEL at 0.8 mg/kg/day from the short-term oral study. This value is of the same magnitude as the NOAEL of 1.0 mg/kg/day from the chronic oral study.

In deriving an ADI value for decabromodiphenyl ether from the chronic NOAEL of 1.0 mg/kg/day, an uncertainty factor of 100 must be applied to use animal data for human risk assessment and to protect the more sensitive individuals of a population. This corresponds to an ADI value of 0.01 mg/kg/day or 0.7 mg/day for a 70 kg human. Since decabromodiphenyl ether is very insoluble in aqueous media (20-30 ppb) (Norris et al., 1973), the physical form of the compound, the size of the crystals and the co-administration of non-aqueous solvents such as oils may affect the absorption and toxicity of this compound. Without more extensive data on the absorption of decabromodiphenyl ether under conditions other than those used in the feeding studies described above, the ADI of 0.7 mg/day should be considered with caution.

In a 90-day subchronic oral study, pentabromodiphenyl ether and octabromodiphenyl ether induced liver enzymes of male rats at levels as low as 0.78 µmol/kg/day (equivalent doses of 0.44 mg pentabromodiphenyl ether/kg/day and 0.62 mg octabromodiphenyl ether/kg/day); no histological effects on the liver were observed at doses of 0, 0.78, 1.56 or 3.13 µmol/kg/day (Carlson, 1980a). Due to the uncertain relevance of liver induction to health effects, the NOAEL for both compounds is equated with the LOEL of 0.78 µmol/kg/day. In deriving an ADI value for both pentabromodiphenyl ether and octabromodiphenyl ether, an uncertainty factor of 1000 is applied to convert from subchronic to chronic exposure, to use animal data for human

risk assessment, and to protect the more sensitive individuals of a population. This corresponds to an ADI value for pentabromodiphenyl ether of 0.00044 mg/kg/day or 0.031 mg/day for a 70 kg man and an ADI value for octabromodiphenyl ether of 0.00062 mg/kg/day or 0.043 mg/day for a 70 kg man.

The lack of pertinent data precludes risk assessment for p-bromodiphenyl ether, p,p'-dibromodiphenyl ether, tribromodiphenyl ether, tetrabromodiphenyl ether, hexabromodiphenyl ether and nonabromodiphenyl ether.

9. REFERENCES

AIHA (American Industrial Hygiene Association). 1981. Workplace environmental exposure level guide: Decabromodiphenyl oxide. Am. Ind. Hyg. Assoc. J. 42(2): A76-A77.

Applegate, V.C., J.H. Howell, A.E. Hall, Jr. and M.A. Smith. 1957. Toxicity of 4,346 Chemicals to Larval Lampreys and Fishes. Spec. Sci. Rep. Fish No. 207, Fish Wildl. Serv., U.S.D.I., Washington, DC. (Cited in U.S. EPA, 1983)

Branson, D.R. 1977. A new capacitor fluid - A case study in product stewardship. Aquatic Toxicology and Hazard Evaluation. ASTM Special Techn. Publ. No. 634, F.L. Mayer and J.L. Hamelink, Ed. Am. Soc. Test. Mater., Philadelphia, PA. p. 44-61. (Cited in Callahan et al., 1979)

Buccafusco, R.J., S.J. Ells and G.A. LeBlanc. 1981. Acute toxicity of priority pollutants to bluegill Lepomis macrochirus. Bull. Environ. Contam. Toxicol. 26(4): 446-452.

Callahan, M.A., M.W. Slimak, N.W. Gabel, et al. 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Vol. 2: Halogenated Aliphatic Hydrocarbons, Halogenated Ethers, Monocyclic Aromatic, Phthalate Esters, Polycyclic Aromatic Hydrocarbons, Nitrosamines, Miscellaneous Compounds. EPA 440/4-79-029b.

Carlson, G.P. 1980a. Induction of xenobiotic metabolism in rats by brominated diphenyl ethers administered for 90 days. Toxicol. Lett. 6(3): 207-212.

Carlson, G.P. 1980b. Induction of xenobiotic metabolism in rats by short-term administration of brominated diphenyl ethers. Toxicol. Lett. 5(1): 19-26.

DeCarlo, V.J. 1979. Studies on brominated chemicals in the environment. Ann. NY Acad. Sci. 320: 678-681.

Dorfman, L.M. and G.E. Adams. 1973. Reactivity of the hydroxyl radical in aqueous solution. NSRDS-NBS-46. NTIS COM-73-50623. (Cited in Callahan et al., 1979)

Kociba, R.J., L.O. Frauson, C.G. Humiston, et al. 1975. Results of a two-year dietary feeding study with decabromodiphenyl oxide (DBDPO) in rats. J. Combust. Toxicol. 2(4): 267-285.

Koster, P., F.M.H. Debets and J.J.T.W.A. Strik. 1980. Porphyrinogenic action of fire retardants. Bull. Environ. Contam. Toxicol. 25(2): 313-315.

Larson, E.R. 1979. Flame retardants (halogenated). In: Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed., Vol. 10, M. Grayson and D. Echroth, Ed. John Wiley and Sons, Inc., NY. p. 384-385.

LeBlanc, G.A. 1980. Acute priority pollutants to water flea (Daphnia magna). Bull. Environ. Contam. Toxicol. 24(5): 684-691.

Leo, A., C. Hansch and D. Elkins. 1971. Partition coefficients and their uses. Chem. Rev. 71: 525-612. (Cited in Callahan et al., 1979)

Mabey, W.R., J.H. Smith, R.T. Podoll, et al. 1982. Aquatic fate process data for organic priority pollutants. Off. Water Regul. Stand., Washington, DC. EPA 440/4-81-014.

NIOSH (National Institute of Occupational Safety and Health). 1983. RTECS (Registry of Toxic Effects of Chemical Substances). February, 1983: Online.

Norris, J.M., J.W. Ehrmantraut, C.L. Gibbons, et al. 1973. Toxicological and environmental factors involved in the selection of decabromodiphenyl oxide as a fire retardant chemical. Appl. Polym. Symp. 22: 195-219.

Norris, J.M., R.J. Kociba, B.A. Schwetz, et al. 1975. Toxicology of octabromodiphenyl and decabromodiphenyl oxide. Environ. Health Perspect. 11: 153-161.

NTP (National Toxicology Program). 1982. Carcinogenesis Testing Program. Chemicals in Standard Protocol. Management Status. Rep. dated: December 31.

Patterson, J.W. and P.S. Kodukala. 1981. Biodegradation of Hazardous Organic Pollutants. CEP, April. p. 48-55.

SRI International. 1983. Directory of Chemical Producers. United States of America. SRI International. Menlo Park, CA.

Tabak, H.H., S.A. Quave, C.I. Mashni and E.F. Barth. 1981. Biodegradability studies with organic priority pollutant compounds. J. Water Pollut. Control Fed. 53: 1503-1518.

Theiss, J.C., G.D. Stoner, M.B. Shimkin and E.K. Weisburger. 1977. Test for carcinogenicity of organic contaminants of United States drinking waters by pulmonary tumor response in strain A mice. Cancer Res. 37(8): 2717-2720.

U.S. EPA. 1977. TSCA (Toxic Substances Control Act). Plant and production search system. Searched through CIS. February, 1983.

U.S. EPA. 1978. In-depth studies on health and environmental impacts of selected water pollutants. Contract No. 68-01-4646.

U.S. EPA. 1980a. Treatability Manual, Vol. I. Treatability Data. July, 1980. EPA 600/8-80-042a. (Cited in Patterson and Kodukala, 1981)

U.S. EPA. 1980b. Ambient Water Quality Criteria Document for Haloethers. Environmental Criteria and Assessment Office, Cincinnati, OH. EPA 440/5-80-050. NTIS PB 296 796.

U.S. EPA. 1983. AQUIRE: Aquatic Information Retrieval Database. March 18.

Weast, R.C., Ed. 1977. Handbook of Chemistry and Physics, 58th ed. CRC Press, Inc., Cleveland, OH. p. 2398.

Yagi, O. and R. Sudo. 1980. Degradation of polychlorinated biphenyls by microorganisms. J. Water Pollut. Control Fed. 52(5): 1035-1043.

APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of:

CA SEARCH (Files 308, 309, 310, 311, 320)
TOXLINE
MEDLINE
RTECS
SCI SEARCH
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
EPCASR
Chemical Industry Notes

Most of these searches were conducted in February, 1983; a few were conducted March-May, 1983. In addition, hand searches were made of Chemical Abstracts (Collective Indices 7 and 8th), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. TLVs: Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981). Cincinnati, OH. p. 486.

ACGIH (American Conference of Governmental Industrial Hygienists). 1982. Documentation of the Threshold Limit Values for Chemical Substances in Work Air. Cincinnati, OH. p. 94.

Bruin, P., G.J. Bergen and J.J. Desta, Eds. 1980. Handling Chemicals Safely, 2nd ed. Dutch Assoc. of Safety Experts, Dutch Chemical Industry Assoc. and Dutch Safety Institute, The Netherlands. p. 1013.

Clayton, G.D. and F.E. Clayton, Eds. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A. John Wiley and Sons, NY. p. 2878.

Clayton, G.D. and F.E. Clayton, Eds. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev ed., Vol. 2B. John Wiley and Sons, NY. p. 2879-3816.

Clayton, G.D. and F.E. Clayton, Eds. 1982. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C. John Wiley and Sons, NY. p. 3817-5112.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., MA. p. 575.

ITII (International Technical Information Institute). 1982. Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data. ITII, Tokyo, Japan. p. 700.

Muir, G.D., Ed. 1977. Hazards in the Chemical Laboratory, 2nd ed. The London Chemical Society, London. p. 473.

NTP (National Toxicology Program). 1982. Carcinogenesis Testing Program. Chemicals on Standard Protocol. Management Status. Rep. date: December 31.

Proctor, N.H. and J. P. Hughes. 1978. Chemical Hazards of the Workplace. J.B. Lippincott Co., Philadelphia. p. 533.

Sax, I.N. 1979. Dangerous Properties of Industrial Materials, 5th ed. Van Nostrand Reinhold Co., NY.